

REMARKS

Favorable reconsideration, reexamination, and allowance of the present patent application are respectfully requested in view of the foregoing amendments and the following remarks. The foregoing amendments have full support in the specification, at least, at paragraphs [0039], [0047], [0053], and [0103] of the published patent application 2007/0130628. No new matter is entered.

Amendments

Claims 1 and 3 have been amended.

Rejection under 35 U.S.C. § 112, second paragraph

In the Office Action, beginning at page 2, claims 1-5, 7, 8, 18-23 and 25-29 were rejected under 35 U.S.C. § 112, second paragraph, as reciting subject matters that allegedly are indefinite. Applicant respectfully requests reconsideration of this rejection.

Although Applicant does not necessarily agree with the bases for this rejection, particularly as outlined in the previous response filed September 11, 2009, claims 1 and 3 have been amended to overcome this rejection. As a result of these amendments, claims 1 and 3 clearly require the antibody-secreting cells to have the recited features. In particular, in a germline transgenic mouse all of the antibody-secreting cells will be carrying the transgene or transgenes.

For at least the foregoing reasons, Applicant respectfully submits that the claims fully comply with 35 U.S.C. § 112, second paragraph, and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 112.

Rejection under 35 U.S.C. § 103(a)

In the Office Action, beginning at page 4, Claims 1-5, 7, 8, 18-21, 23, 25-27 and 29 were rejected under 35 U.S.C. § 103(a), as reciting subject matters that allegedly are obvious, and therefore allegedly unpatentable, over the disclosure of Zaccolo *et al.* (hereinafter “Zaccolo”), in view of the disclosure of Weissinger *et al.* (hereinafter “Weissinger”), Yu *et al.* (hereinafter “Yu”), and Felsher *et al.* (hereinafter “Felsher”).

Applicant respectfully requests reconsideration of this rejection.

In response to Applicant's previous response filed September 11, 2009, and the arguments made therein regarding the improper hindsight application of the cited references, the current Office Action maintains this rejection on the basis that any judgment on obviousness is necessarily a reconstruction based on hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. It is asserted that the Examiner could not have reconstructed the obviousness determination without the knowledge presented in Applicant's specification.

Therefore, it is respectfully maintained that the Examiner is applying hindsight analysis using not only the knowledge which was within the level of ordinary skill at the time the invention was made, but also necessarily elements from Applicant's disclosure. The Examiner had to select and combine features from four different prior art documents based only on the alleged motivation that Zaccolo implicitly teaches the need for improved methods of immortalization. However, the Examiner has provided no teaching that guides the skilled person to select the appropriate features from the four documents and combine them in such a way as to arrive at the present invention. Specifically, Zaccolo offers no mention or suggestion of using transgenic animals. Weissinger also does not teach or suggest the use of transgenic animals, and is cited for teaching the use of oncogene expression for direct immortalization of antibody-secreting B lymphocytes. Yu is cited for establishing that it was well known in the art to use transgenic mice to directly immortalize B lymphocytes. Felsher is cited for establishing that the use of an inducible expression system which controls the expression of the *myc* gene for reversible tumorigenesis is known in the art.

It is alleged that the person of ordinary skill in the art would have been motivated to modify the method taught by Zaccolo in view of Weissinger because of the need for improved methods of immortalization. Further, the Examiner alleges that it would have been obvious to the person of ordinary skill to select the teachings of Yu and Felsher as the basis for a modification, which would lead them to the present invention.

However, the person of ordinary skill in the art would not have selected the documents and teachings by Yu and Felsher to improve the methods of immortalization as taught by Zaccolo and Weissinger without the knowledge presented in Applicant's specification. This is because there is nothing in Zaccolo or Weissinger and the problems they each identify which would lead the person of ordinary skill to the teachings of Yu and Felsher, which are directed to a completely different field of technology and are discussed *infra*. There is nothing in Yu and Felsher regarding antibody production which would allow the person of ordinary skill to identify these documents ***without a knowledge of the present invention.***

Specifically, neither Zaccolo nor Weissinger suggest the use of a transgenic animal wherein the antibody-secreting cells are capable of expression of one or more transgenes, and are in a nonimmortalized state in the absence of a stimulus but are capable of changing to an immortalized state by means of the transgene upon exposure of the cells to the stimulus. Furthermore, the disclosures of both Yu and Felsher are related to the study of cancer and are not concerned with the issue of antibody production.

The study reported by Yu relates to the generation of a non-transgenic mouse model of B-lymphoma to address the specific question as to whether Myc-over-expressing, p53-null B-cell precursors are immediately tumorigenic in syngeneic mice (see page 1923, right hand column, end of first paragraph). In particular, the authors are concerned with further understanding the involvement of *c-myc* in haematopoietic tumors. Clearly, this has nothing to do with antibody production, nor the achieving an immortalized state by means of a transgene upon exposure of the cells to a stimulus, and therefore, cannot be combined with the teachings of Zaccolo or Weissinger, in particular without knowledge of that disclosed in Applicant's specification.

Turning to Felsher, this document is also concerned with oncology and the question of whether targeted repair of mutant protooncogenes or the inactivation of their gene products may be a specific and effective therapy for human neoplasia (see abstract). To investigate this issue, the authors generate transgenic mice that conditionally express the *myc* protooncogene in hematopoietic cells. The authors demonstrate that sustained expression of the *myc* transgene culminated in the formation of malignant T cell lymphomas and acute myeloid leukemias, while the subsequent inactivation of the

transgene causes regression of the established tumours. Neither Yu nor Felsher discusses or suggests antibody production.

Accordingly, the combination of the teachings of Zaccolo, Weissinger, Yu and Felsher would not have been made by the person skilled in the art at the priority date of the invention. Such a combination can only be made in hindsight, with the benefit of the knowledge of the present invention. Clearly, the disparate teachings of these four references cannot be combined to render the claimed invention obvious, in that the person of ordinary skill in the art would have no reason, suggestion, or logical rationale to combine their disparate teachings. Yu and Felsher deal exclusively with oncogenesis and the study of cancer, whereas the Zaccolo and Weissinger merely teach old technology in the study of immortalization of antibody-secreting cells. For these reasons, the combination of references as cited cannot render the claimed invention obvious.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007). Clearly, the claimed invention does not yield results which were predictable based on the teachings of the prior art. With the method of the present invention, all the antibody-secreting cells from a single mouse can be immortalized on demand, giving rise to greater antibody diversity. This effect, and how to obtain it, is entirely surprising in view of the prior art, and is only obvious with the knowledge of the present invention. There is no way that the combination of the four cited references would suggest such a result to the ordinarily skilled art worker.

For at least the foregoing reasons, Applicant respectfully submits that the subject matters of claims each taken as a whole, would not have been obvious to one of ordinary skill in the art at the time of Applicant's invention, are therefore not unpatentable under 35 U.S.C. § 103(a), and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 103(a).

Conclusion

For at least the foregoing reasons, Applicant respectfully submits that the present patent application is in condition for allowance. An early indication of the allowability of the present patent application is therefore respectfully solicited.

If Examiner Li believes that a telephone conference with the undersigned would expedite passage of the present patent application to issue, she is invited to call on the number below.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is hereby authorized to charge fees necessitated by this paper, and to credit all refunds and overpayments, to our Deposit Account 50-2821.

Respectfully submitted,

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